

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants:   Samy Ashkar

Serial No.:   Divisional of 08/918,189

Art Unit:     Not Yet Assigned

Filed:        December 22, 2003

Examiner:    Not Yet Assigned

For:           *NOVEL OSTEOPONTIN DERIVED CHEMOTACTIC PEPTIDES AND  
METHODS OF USE*

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**INFORMATION DISCLOSURE STATEMENT**

Sir:

Pursuant to 37 C.F.R. §1.56 and 37 C.F.R. §1.97, Applicant submits an Information Disclosure Statement, including five (5) pages of Form PTO-1449. All of the documents cited below were cited by or submitted to the Patent Office in Application Serial No. 08/918,189, filed August 21, 1997, to which the present application claims priority. Pursuant to 37 C.F.R. §1.98(d), Applicants are not enclosing copies of these publications. Copies will be provided upon request, however.

This Information Disclosure Statement is being filed under 37 C.F.R. § 1.97(b) prior to a first Office Action on the merits. It is believed that no fee is required with this submission. However, should a fee be required, the Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-1868.

### U.S. Patents

<u>Number</u>	<u>Issue Date</u>	<u>Patentee</u>	<u>Class/Subclass</u>
4,693,718	09-15-1987	Urry, et al.	623/11
4,976,734	12-11-1990	Urry, et al.	623/11
5,519,003	03-21-1996	Mochly-Rosen	514/16
5,773,569	06-30-1998	Wrighton, et al.	530/300
5,989,553	11-23-1999	Johnston	424/190.1

### Foreign Documents

<u>Number</u>	<u>Publication Date</u>	<u>Patentee</u>	<u>Country</u>
0 269 595	07-14-1993	Erlansen-Albertsson	EP

### Publications

BEHREND, et al., "Reduced malignancy of *ras*-transformed NIH 3T3 cells expressing antisense osteopontin RNA," *Cancer Res.* 54: 832-837 (1994).

CHAMBERS, et al., Induction of expression of osteopontin (OPN; secreted phosphoprotein) in metastatic, *ras*-transformed NIH 3T3 cells," *Anticancer Res.* 12: 43-47 (1992).

CRAIG, et al., "Secreted phosphoprotein mRNA is induced during multi-stage carcinogenesis in mouse skin and correlates with the metastatic potential of murine fibroblasts," *Int. J. Cancer* 46: 133-137 (1990).

DENHARDT & GUO, "Osteopontin: a protein with diverse functions," *FASEB J.* 7: 1475-1482 (1993).

FOLKMAN, "What is the role of endothelial cells in angiogenesis?" *Lab. Invest.* 51(6): 601-604 (1984).

GIACHELLI, et al., "Molecular cloning and characterization of 2B7, a rat mRNA which distinguishes smooth muscle cell phenotypes in vitro and is identical to osteopontin (secreted phosphoprotein I, 2aR)," *Biochem. Biophys. Res. Commun.* 177(2): 867-873 (1991).

GÜNTHERT, et al., "A new variant of glycoprotein CD44 confers metastatic potential to rat carcinoma cells," *Cell* 65: 13-24 (1991).

KIEFER, et al., "The cDNA and derived amino acid sequence for human osteopontin," *Nucl. Acids Res.* 17(8): 3306 (1989).

KUBOTA, et al., "Multiple formes of SPPI (secreted phosphoprotein, osteopontin) synthesized by normal and transformed rat bone cell populations: regulation by TGF- $\beta$ ," *Biochem. Biophys. Res. Comm.* 162(3): 1453-1459 (1989).

LAMPE, et al., "Polyclonal B cell activation by the Eta-1 cytokine and the development of systemic autoimmune disease," *J. Immunol.* 147(9): 2902-2906 (1991).

LIAW, et al., "Osteopontin promotes vascular cell adhesion and spreading and is chemotactic for smooth muscle cells in vitro," *Circ. Res.* 74: 214-224 (1994).

LOMBARDI, et al., "Neutralizing antibodies directed against osteopontin inhibit FMLP induced macrophage infiltration in rat skin," *FASEB J.* 10(6): a1293, Abst. #1694 (1996).

NASU, et al., "Expression of wild-type and mutated rabbit osteopontin in *Escherichia coli*, and their effects on adhesion and migration of P388D1 cells," *Biochem. J.* 307: 257-265 (1995).

OLDBERG, et al., "Cloning and sequence analysis of rat bone sialoprotein (osteopontin) cDNA reveals and Arg-Gly-Asp cell-binding sequence," *Proc. Natl. Acad. Sci USA* 83: 8819-8823 (1986).

OLDBERG, et al., "Identification of a bone sialoprotein receptor in osteosarcoma cells," *J. Biol. Chem.* 263(36): 19433-19436 (1988).

PATARCA, et al., "Differential induction of interferon  $\gamma$  gene expression after activation of CD4+ T cells by conventional antigen and M1s superantigen," *Proc. Natl. Acad. Sci. USA* 88: 2736-2739 (1991).

PATARCA, et al., "Dysregulated expression of the T cell cytokine *Eta-1* in CD4-8- lymphocytes during the development of murine autoimmune disease," *J. Exp. Med.* 172: 1177-1183 (1990).

PATARCA, et al., "Molecular and cellular basis of genetic resistance to bacterial infection: the role of the early T-lymphocyte activation-1/osteopontin gene," *Crit. Rev. Immunol.* 13(3-4): 225-246 (1993).

PATARCA, et al., "Structural and functional studies of the early T lymphocyte activation 1 (*Eta-1*) gene," *J. Exp. Med.* 170: 145-161 (1989).

PETTERSON, et al., "Synthesis, NMR and function of an O-phosphorylated peptide, comprising the RGD-adhesion sequence of osteopontin," *Acta Chem. Scand.* 45: 604-608 (1991).

RODAN, "Osteopontin overview," *Ann. NY Acad. Sci.* 1-5 (1995).

SEITER, et al., "Prevention of tumor metastasis formation by anti-variant CD44," *J. Exp. Med.* 177: 443-455 (1993).

SENGER, et al., "Adhesive properties of osteopontin: regulation by a naturally occurring thrombin-cleavage in close proximity to the GRGDS cell-binding domain," *Mol. Biol. Cell* 5: 565-574 (1994).

SENGER, et al., "Elevated expression of secreted phosphoprotein I (osteopontin, 2ar) as a consequence of neoplastic transformation," *Anticancer Res.* 9: 1291-1299 (1989).

SINGH, et al., "Definition of a specific interaction between the early T lymphocyte activation 1 (Eta-1) protein and murine macrophages in vitro and its effect upon macrophages in vivo," *J. Exp. Med.* 171: 1931-1942 (1990).

SMITH & DERNHARDT, "Molecular cloning of a tumor promoter-inducible mRNA found in JB6 mouse epidermal cells: induction is stable at high, but not at low, cell densities," *J. Cell. Biochem.* 34: 13-22 (1987).

SØRENSEN & PETERSEN, "Identification of two phosphorylation motifs in bovine osteopontin," *Biochem. Biophys. Res. Comm.* 198(1): 200-205 (1994).

SØRENSEN, et al., "Posttranslational modifications of bovine osteopontin: identification of twenty-eight phosphorylation and three O-glycosylation sites," *Protein Sci.* 4(10): 2040-2049 (1995).

ULLRICH, et al., "Biosynthesis and secretion of an osteopontin-related 20kDa polypeptide in the Madin-Darby canine kidney cell line," *J. Biol. Chem.* 266(6): 3518-3525 (1991).

VAN DIJK, et al., "Evidence that a non-RGD domain in rat osteopontin is involved in cell attachment," *J. Bone Min. Res.* 8(12): 1499-1506 (1993).

WEBER, et al., "Receptor-ligand interaction between CD44 and osteopontin (Eta-1)," *Science* 271: 509-512 (1996).

XUAN, et al., "Site-directed mutagenesis of the RGD sequence in osteopontin destroys cell adhesion and migration functions," *J. Cell. Biochem.* 57: 680-690 (1995).

YAMAMOTO, et al., "Effect of recombinant osteopontin on adhesion and migration of P388D1 cells," *Ann. NY Acad. Sci.* 760: 378-380 (1995).

YOUNG, et al., "cDNA cloning, mRNA distribution and heterogeneity, chromosomal location, and RFLP analysis of human osteopontin (OPN)," *Genomics* 7: 491-502 (1990).

YUE, et al., "Osteopontin-stimulated vascular smooth muscle cell migration is mediated by  $\beta_3$  integrin," *Exp. Cell Res.* 214: 459-464 (1994).

Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				Applicant Number	Divisional f08/918,189
				Filing Date	December 22, 2003
				First Named Inventor	Samy Ashkar
				Group Art Unit	
				Examiner Name	
				Attorney Docket Number	CMCC 512 DIV
Sheet	1	of	5		

[illegible][illegible]

Examine Signature		Date Considered	
-------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to application.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SENT TO: Assistant Commissioner for Patent, Washington, DC 20231.

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-96)  
Approved for use through 10/31/99. OMB 0651-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

<b>Substitute for form 1449A/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Completing Information</b>		
				<b>Application Number</b>		<b>Divisional 108/918,189</b>
				<b>Filing Date</b>		<b>December 22, 2003</b>
				<b>First Named Inventor</b>		<b>Samy Ashkar</b>
				<b>Group Art Unit</b>		
				<b>Examiner Name</b>		
<b>Sheet</b>	<b>2</b>	<b>of</b>	<b>5</b>	<b>Attorney Docket Number</b>		<b>CMCC 512 DIV</b>

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		BEHREND, et al., "Reduced malignancy of <i>ras</i> -transformed NIH 3T3 cells expressing antisense osteopontin RNA," <i>Cancer Res.</i> 54: 832-837 (1994).	
		CHAMBERS, et al., Induction of expression of osteopontin (OPN; secreted phosphoprotein) in metastatic, <i>ras</i> -transformed NIH 3T3 cells," <i>Anticancer Res.</i> 12: 43-47 (1992).	
		CRAIG, et al., "Secreted phosphoprotein mRNA is induced during multi-stage carcinogenesis in mouse skin and correlates with the metastatic potential of murine fibroblasts," <i>Int. J. Cancer</i> 46: 133-137 (1990).	
		DENHARDT & GUO, "Osteopontin: a protein with diverse functions," <i>FASEB J.</i> 7: 1475-1482 (1993).	
		FOLKMAN, "What is the role of endothelial cells in angiogenesis?" <i>Lab. Invest.</i> 51(6): 601-604 (1984).	
		GIACHELLI, et al., "Molecular cloning and characterization of 2B7, a rat mRNA which distinguishes smooth muscle cell phenotypes in vitro and is identical to osteopontin (secreted phosphoprotein I, 2aR)," <i>Biochem. Biophys. Res. Commun.</i> 177(2): 867-873 (1991).	
		GÜNTHER, et al., "A new variant of glycoprotein CD44 confers metastatic potential to rat carcinoma cells," <i>Cell</i> 65: 13-24 (1991).	
		KIEFER, et al., "The cDNA and derived amino acid sequence for human osteopontin," <i>Nucl. Acids Res.</i> 17(8): 3306 (1989).	
		KUBOTA, et al., "Multiple forms of SPPI (secreted phosphoprotein, osteopontin) synthesized by normal and transformed rat bone cell populations: regulation by TGF- $\beta$ ," <i>Biochem. Biophys. Res. Comm.</i> 162(3): 1453-1459 (1989).	
		LAMPE, et al., "Polyclonal B cell activation by the Eta-1 cytokine and the development of systemic autoimmune disease," <i>J. Immunol.</i> 147(9): 2902-2906 (1991).	

<b>Examiner's Signature</b>		<b>Date Considered</b>	
-----------------------------	--	------------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO				Completeness	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				Applicant Number	
				Divisional of 08/918,189	
				Filing Date	
				December 22, 2003	
				First Named Inventor	
				Samy Ashkar	
Group Art Unit					
Examiner Name					
Sheet	3	of	5	Attorney Docket Number	
				CMCC 512 DIV	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		LIAW, et al., "Osteopontin promotes vascular cell adhesion and spreading and is chemotactic for smooth muscle cells in vitro," <i>Circ. Res.</i> 74: 214-224 (1994).	
		LOMBARDI, et al., "Neutralizing antibodies directed against osteopontin inhibit FMLP induced macrophage infiltration in rat skin," <i>FASEB J.</i> 10(6): a1293, Abst. #1694 (1996).	
		NASU, et al., "Expression of wild-type and mutated rabbit osteopontin in <i>Escherichia coli</i> , and their effects on adhesion and migration of P388D1 cells," <i>Biochem. J.</i> 307: 257-265 (1995).	
		OLDBERG, et al., "Cloning and sequence analysis of rat bone sialoprotein (osteopontin) cDNA reveals and Arg-Gly-Asp cell-binding sequence," <i>Proc. Natl. Acad. Sci. USA</i> 83: 8819-8823 (1986).	
		OLDBERG, et al., "Identification of a bone sialoprotein receptor in osteosarcoma cells," <i>J. Biol. Chem.</i> 263(36): 19433-19436 (1988).	
		PATARCA, et al., "Differential induction of interferon $\gamma$ gene expression after activation of CD4+ T cells by conventional antigen and M1s superantigen," <i>Proc. Natl. Acad. Sci. USA</i> 88: 2736-2739 (1991).	
		PATARCA, et al., "Dysregulated expression of the T cell cytokine <i>Eta-1</i> in CD4-8-lymphocytes during the development of murine autoimmune disease," <i>J. Exp. Med.</i> 172: 1177-1183 (1990).	
		PATARCA, et al., "Molecular and cellular basis of genetic resistance to bacterial infection: the role of the early T-lymphocyte activation-1/osteopontin gene," <i>Crit. Rev. Immunol.</i> 13(3-4): 225-246 (1993).	
		PATARCA, et al., "Structural and functional studies of the early T lymphocyte activation 1 ( <i>Eta-1</i> ) gene," <i>J. Exp. Med.</i> 170: 145-161 (1989).	
		PETTERSON, et al., "Synthesis, NMR and function of an O-phosphorylated peptide, comprising the RGD-adhesion sequence of osteopontin," <i>Acta Chem. Scand.</i> 45: 604-608 (1991).	

Examiner's Signature		Date Considered	
----------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-96)  
Approved for use through 10/31/99. OMB 0651-0031  
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

+

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

<p>Substitute for form 1449A/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p>(use as many sheets as necessary)</p>		<b>Complete if Known</b>	
		Application Number	Divisional of 08/918,189
		Filing Date	December 22, 2003
		First Named Inventor	Samy Ashkar
		Group Art Unit	
		Examiner Name	
Sheet 4 of 5	Attorney Docket Number	CMCC 512 DIV	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		RODAN, "Osteopontin overview," <i>Ann. NY Acad. Sci.</i> 1-5 (1995).	
		SEITER, et al., "Prevention of tumor metastasis formation by anti-variant CD44," <i>J. Exp. Med.</i> 177: 443-455 (1993).	
		SENGER, et al., "Adhesive properties of osteopontin: regulation by a naturally occurring thrombin-cleavage in close proximity to the GRGDS cell-binding domain," <i>Mol. Biol. Cell</i> 5: 565-574 (1994).	
		SENGER, et al., "Elevated expression of secreted phosphoprotein I (osteopontin, 2ar) as a consequence of neoplastic transformation," <i>Anticancer Res.</i> 9: 1291-1299 (1989).	
		SINGH, et al., "Definition of a specific interaction between the early T lymphocyte activation 1 (Eta-1) protein and murine macrophages in vitro and its effect upon macrophages in vivo," <i>J. Exp. Med.</i> 171: 1931-1942 (1990).	
		SMITH & DERNHARDT, "Molecular cloning of a tumor promoter-inducible mRNA found in JB6 mouse epidermal cells: induction is stable at high, but not at low, cell densities," <i>J. Cell. Biochem.</i> 34: 13-22 (1987).	
		SØRENSEN & PETERSEN, "Identification of two phosphorylation motifs in bovine osteopontin," <i>Biochem. Biophys. Res. Comm.</i> 198(1): 200-205 (1994).	
		SØRENSEN, et al., "Posttranslational modifications of bovine osteopontin: identification of twenty-eight phosphorylation and three O-glycosylation sites," <i>Protein Sci.</i> 4(10): 2040-2049 (1995).	
		ULLRICH, et al., "Biosynthesis and secretion of an osteopontin-related 20kDa polypeptide in the Madin-Darby canine kidney cell line," <i>J. Biol. Chem.</i> 266(6): 3518-3525 (1991).	
		VAN DIJK, et al., "Evidence that a non-RGD domain in rat osteopontin is involved in cell attachment," <i>J. Bone Min. Res.</i> 8(12): 1499-1506 (1993).	

Examiner's Signature		Date Considered	
----------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+



Please type a plus sign (+) inside this box →



+

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

<p>Substitute for form 1449A/PTO</p> <p><b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b></p> <p>(use as many sheets as necessary)</p>		<b>Complete If Known</b>	
		Application Number	Divisional of 08/918,189
		Filing Date	December 22, 2003
		First Named Inventor	Samy Ashkar
		Group Art Unit	
		Examiner Name	
Sheet 5 of 5	Attorney Docket Number	CMCC 512 DIV	

OTHER ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T <sup>2</sup>
		WEBER, et al., "Receptor-ligand interaction between CD44 and osteopontin (Eta-1)," <i>Science</i> 271: 509-512 (1996).	
		XUAN, et al., "Site-directed mutagenesis of the RGD sequence in osteopontin destroys cell adhesion and migration functions," <i>J. Cell. Biochem.</i> 57: 680-690 (1995).	
		YAMAMOTO, et al., "Effect of recombinant osteopontin on adhesion and migration of P388D1 cells," <i>Ann. NY Acad. Sci.</i> 760: 378-380 (1995).	
		YOUNG, et al., "cDNA cloning, mRNA distribution and heterogeneity, chromosomal location, and RFLP analysis of human osteopontin (OPN)," <i>Genomics</i> 7: 491-502 (1990).	
		YUE, et al., "Osteopontin-stimulated vascular smooth muscle cell migration is mediated by $\beta_3$ integrin," <i>Exp. Cell Res.</i> 214: 459-464 (1994).	

Examiner's Signature		Date Considered	
----------------------	--	-----------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Unique citation designation number <sup>2</sup> See attached Kinds of U.S. Patent Documents. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+